REMARKS

Applicants have amended claim 1 and added new claim 32 to more particularly point out and more distinctly claim a method of recovering mesenchymal stem cells (MSCs). Support for this amendment can be found at page 8, line 28 to page 9, line 10. Applicants have also amended claims 4-6 to promote clarity. Note that Applicants already cancelled claims 2, 8, 21, 22, and 24-31 in the response to a previous office action, and withdrew claims 12-20 drawn to a non-elected invention in the response to the restriction requirement.

Claims 1, 3-7, 9-11, 23 and 32 are currently being examined. Reconsideration of the application, as amended, is respectfully requested in view of the remarks below.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 1, 3-7, 9-11, and 23 as being obvious over Rieser et al., U.S. Patent 6,242,247 ("Rieser") in view of Bruder et al., U.S. Patent 5,942,225 ("Bruder") and Huss, U.S. Patent 6,361,997 ("Huss"). See the Office Action, page 3, line 19 to page 4, line 2.

Claim 1, the only pending independent claim, is drawn to a method for recovering MSCs from other cells, based on their different sizes. The method includes (a) providing a cell mixture which contains MSCs and other cells, (b) seeding the mixture into a device containing an upper plate with pores and a lower plate base, so as to physically separate MSCs (which adhere to the upper plate due to their larger size) from other cells (which pass through the pores to the lower plate base due to their smaller size), and (c) recovering the MSCs from the upper plate.

As correctly pointed out by the Examiner, the primary reference "Rieser et al teach a method of making implants comprising culturing cells capable of chondrocyte-function, including mesenchymal stem cells (MSCs), in a culture device comprising a porous plate." See the Office Action, page 4, lines 3-5. Applicants note a key difference between the device recited in claim 1 and the Rieser device. Specifically, the Rieser device contains a cell space surrounded partly by a semi-permeable wall (which is permeable to culture media but not cells) and partly by a plate located underneath the cell space (which is also not permeable to cells and allows the cells to settle on it). See the Abstract and Figure 2. In other words, the Rieser device solely serves the purpose of culturing cells, not physically separating cells, as required by claim 1.

This deficiency in Rieser, as discussed below, is not cured by the two secondary references relied on by the Examiner, i.e., Bruder and Huss.

Bruder discloses a method for lineage-directed induction of isolated, culture expanded human MSCs. As correctly pointed out by the Examiner, Bruder teaches isolating human MSCs and culturing them in a specially prepared medium, i.e., DMEM-LG. See the Office Action, page 4, lines 12-13. The DMEM-LG medium allows "for the direct adherence of only the mesenchymal stem cells to the plastic or glass surface of the culture vessel." See Bruder, column 4, lines 26-30. The device recited in claim 1, as mentioned above, allows one to physically separate MSCs from other cells. By contrast, in the Bruder method, both MSCs and other cells are kept in the medium even though only the former are attached to the culture vessel. Further, the Bruder method selects MSCs based on their biochemical characteristics (i.e., adherence), not their physical characteristics (i.e., size) as required by claim 1.

Huss teaches gene and cell therapy using genetically modified cells, e.g., MSCs that are CD34 negative. See column 1, lines 7-11. According to the Examiner, "Huss demonstrates that mesenchymal stem cells that adhere to the culture surface are CD34-negative." See the Office Action, page 4, lines 16-17. This teaching is a far cry from physically separating MSCs from other cells as required by claim 1.

For the reasons set forth above, Applicants submit that neither Bruder nor Huss suggests a method that physically separates MSCs from other cells. Both references fail to provide what is lacking from Rieser. In other words, the Examiner has not established a prima facie case of obviousness.

Even assuming that the Examiner has done so (which Applicants do not concede), the prima facie obviousness can be successfully rebutted by a showing of an unexpected property of the MSCs recovered by the method of claim 1. More specifically, MSCs cultured by conventional technique require 14-21 days to reach confluence (U.S. Patent 5,486,359, attached hereto as "Exhibit A," column 10, lines 21-23), yet MSCs recovered by the method of claim 1 only require 10 days to reach confluence. See the Specification, page 14, lines 21-22. These unexpected results have successfully rebutted any presumption of obviousness based on the cited references.

In view of the above remarks, Applicants submit that claim 1 is not rendered obvious by Rieser, alone or in combination with Bruder or Huss. Neither are claims 3-7, 9-11, 23 and 32, all of which depend from claim 1.

CONCLUSION

Applicants submit that the grounds for the rejection asserted by the Examiner have been successfully overcome, and that claims 1, 3-7, 9-11, 23 and 32, as pending, define subject matter that is definite, novel, and nonobvious over the prior art. Based on the remarks set forth above, Applicants submit that all claims cover allowable subject matter, and should be allowed. Early allowance by the Examiner is respectfully solicited.

Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges to deposit account 06-1050, referencing Attorney's Docket No: 14558-002US1.

Respectfully submitted,

Date: 3-18-05

Y. Rocky Tsao, Ph.D., J.D.
Attorney for Applicant
Registration No. 34,053

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906